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Michael O. Leavitt, Administrator
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Comments on the HPV test plan for 1H-isoindole-1,3(2H)-dione, 5,5'-[(methylethylidene) bis (4,1-phenyleneoxy)] bis [2-methyl]

Dear Administrator Leavitt:

The following comments on General Electric's test plan for 1H-isoindole-1,3(2H)-dione, 5,5'-[(methylethylidene) bis (4,1-phenyleneoxy)] bis [2-methyl], or bisphenol A bisimide (BPA-BI; CAS no. 54395-52-7), are submitted on behalf of People for the Ethical Treatment of Animals, the Physicians Committee for Responsible Medicine, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health, and environmental protection organizations have a combined membership of more than ten million Americans.

General Electric's test plan is completely unacceptable. The test plan states that a mammalian reproductive toxicity test is to be carried out (p. 4). However, the robust summary states that **this test is already in progress (p. 24). This is a blatant violation of both the 1999 animal welfare agreement and the HPV framework agreement to which all HPV participants agreed to adhere.** The EPA and the public are to be provided with the opportunity to comment on all test plans and sponsors are to consider those comments before any experimental work is undertaken. The reproductive toxicity test (OECD no. 421) spells suffering and death for at least 675 animals.

There are a number of reasons why the reproductive toxicity study was unnecessary, which further reinforce the inappropriateness of General Electric's failure to wait for public comments:

1. The test plan states that BPA-BI is "a chemical intermediate" (p. 3), but it is unclear whether or not this means it is a closed-system intermediate, and no further information is provided in the robust summary. If BPA-BI is a closed-system intermediate, then, according to the EPA, repeated-dose and reproductive toxicity tests are not required (Wayland 1999, *Federal Register* 2000).
2. Some data about the male and female sex organs were obtained in the rat repeated-dose study (robust summary, p. 23). This information should have been combined with information from the two developmental toxicity tests classified as "reliable without restriction." GE might then have been able to use a weight of evidence approach similar to that recommended by both the EPA and the OECD which states in its Manual for Investigation of HPV Chemicals that when repeated dose studies which include the effects of reproductive organs and a developmental study are available, "the requirements for the reproduction toxicity endpoint would be satisfied" (Chapter 4).

3. General Electric appears to have made no attempt to categorize BPA-BI with related compounds, or to carry out structure-activity analysis. The HPV test plan for bisphenol A dianhydride was submitted by General Electric on the same date as that for BPA-BI, and the compounds differ only in that BPA-BI has two amino groups where bisphenol A dianhydride has two oxygen atoms, yet General Electric provides no discussion as to whether these two compounds could have been classed together. In addition, bisphenol A has been studied extensively for its estrogenic effects (Ashby 2003, Melnick 2002), as well as for other reasons (Hunt 2003), and General Electric should not have evaluated BPA-BI without considering the extensive database on this component.

In addition to the reproductive toxicity study, General Electric states that an acute fish toxicity test is to be carried out (test plan, p. 4). However, the robust summary has no section on ecotoxicity. A test to determine the partition coefficient of BPA-BI is currently in progress (robust summary, p. 5), and it is premature to propose a fish test when this parameter is not known, as acute fish tests are inappropriate for compounds with log K_{ow} values above 4.2 (EPA, *Federal Register* 2000, p. 81695). A test to determine the stability in water is also in progress (robust summary, p. 4), and low stability could also render a fish test inappropriate. There are also a number of other parameters that could render the fish test unnecessary, including corrosivity and volatility, yet General Electric provides no data on these items.

Finally, although the BPA-BI test plan (pp. 1-4) was posted online on March 2, 2004, the robust summary (pp. 5-32) was not posted or not accessible until June 24, 2004. The failure to submit or post the robust summary until six days before the deadline for public comments further complicates the public's ability to perform a thorough review of this test plan. **The EPA needs to once again clarify the requirements of the HPV program to General Electric and ensure that it abides by them if it is going to participate in the HPV program. General Electric needs to carefully review its consultant's (Toxicology/Regulatory Services Inc.) recommendations since TRS may have a financial incentive for proposing additional testing.**

We would appreciate a response to our specific concerns with this test plan. I can be reached at 757-622-7382, ext. 8001, or via e-mail at JessicaS@peta.org.

Sincerely,

Jessica Sandler
Federal Agency Liaison

References

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